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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/789,489

02/26/2004

Samuel Zalipsky

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EXAMINER

SCHLIENTZ, LEAH H

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

10/10/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/789,489	Applicant(s) ZALIPSKY ET AL.	
	Examiner Leah Schlientz	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 12-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 5/1/08, in reply to the Office Action mailed 2/6/08, is acknowledged and has been entered. Claims 6 and 7 have been amended. Claims 11 and 16-27 have been cancelled. Claims 1-10 and 12-15 are pending and are examined herein on the merits for patentability.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 6/16/08 was filed after the mailing date of the Office Action on 2/6/08. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Arguments

All rejections not reiterated herein have been withdrawn.

Applicant's arguments, with respect to the rejection of claims 1 – 10, 12, 13 and 16 – 25 under 35 U.S.C. 103(a) as being unpatentable over Zalipsky (WO 01/05873, whereby US 6,586,001 is relied upon as equivalent), in view of Watanabe *et al.* (US 5,786,387), in further view of Szebeni *et al.* (*J. Liposome Research*, 2002, 12, p. 165 –

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172), have been fully considered but are not persuasive for reasons set forth hereinbelow.

Applicant's arguments, with respect to the rejection of claims 1 – 10, 12-15 and 16 – 27 under 35 U.S.C. 103(a) as being unpatentable over Zalipsky *et al.* (WO 01/05873), in view of Watanabe *et al.* (US 5,786,387), in further view of Szebeni and Abra *et al.* (US 5,945,122), have been fully considered but are not persuasive for reasons set forth hereinbelow.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1–10, 12, 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zalipsky (WO 01/05873, whereby US 6,586,001 is relied upon as equivalent), in view of Watanabe *et al.* (US 5,786,387), in further view of Szebeni *et al.* (*J. Liposome Research*, 2002, 12, p. 165 – 172), for reasons set forth in the previous Office Action.

Claims 1–10 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zalipsky (WO 01/05873, whereby US 6,586,001 is relied upon as equivalent), in view of Watanabe *et al.* (US 5,786,387), in further view of Szebeni *et al.*

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(*J. Liposome Research*, 2002, 12, p. 165 – 172) and Abra *et al.* (US 5,945,122), for reasons set forth in the previous Office Action.

Applicant argues on pages 6-8 of the Response that the pending claims are directed to methods of reducing liposome-induced complement activation to particular liposome structures that entrap the therapeutics, and that none of the cited references teach such methods. Applicant asserts that Zalipsky does not teach using neutral liposome to encapsulate chemotherapeutic agents while Watanabe and Szebeni fail to teach the particularly claimed neutral liposomal structures. Applicant further argues that Szebeni does not teach anything about the structure of their neutral liposomes other than they lack 2K-PEG-DSPE or HSPG, and that given the clear teaching of the specification that (1) neutral liposomal preparations can induce complement activation and (2) in vitro complement activation does not necessarily correspond to in vivo complement activation. Applicant asserts that there was a long-felt need to reduce complement activation in vivo associated with certain liposomal compositions, and that it was unexpected that the particular neutral liposomes would reduce complement activation.

This is not found to be persuasive. Obviousness does not require absolute predictability, only a reasonable expectation of success. See MPEP 2143.02 I. and II. In the instant case, Szebeni teaches that “negative charge on liposome surface plays a key, if not sole role in complement activation,” and that “Doxil, Doxil placebo and negatively charged liposomes caused severe to lethal cardiopulmonary distress in pigs,

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while neutral vesicles were without effect," therefore there was at least a reasonable expectation of success that the neutral liposomes of Zalipsky or Watanabe would be capable of complement reduction as compared to negatively charged liposomes.

With regard to the argument that there was a long-felt need to reduce complement activation associated with certain liposomal compositions, establishing long-felt need requires objective evidence that an art recognized problem existed in the art for a long period of time without solution. The relevance of long-felt need and the failure of others to the issue of obviousness depends on several factors... the long-felt need must not have been satisfied by another before the invention by applicant. *Newell Companies v. Kenney Mfg. Co.*, 864 F.2d 757, 768, 9 USPQ2d 1417, 1426 (Fed. Cir. 1988). See MPEP 716.04. In the instant case, reduction of complement activation has been realized and achieved using certain liposomal formulations, which is at least shown by the Szebeni reference.

Furthermore, the instant claims do not actually require administration of liposomes in vivo or entrapment of a chemotherapeutic agent, as argued by Applicant. The claims are drawn to a "method of reducing liposome-induced complement activation upon in vivo administration of liposomes containing an entrapped chemotherapeutic agent comprising providing liposomes comprised of a vesicle-forming lipid and between 1-10 mole percent of a neutral lipopolymer." However, the only active step in the claims is "*providing* liposomes comprised of a vesicle-forming lipid and between 1-10 mole percent of a neutral lipopolymer having the formula" shown in claim 1. The "administration in vivo" and "entrapment of chemotherapeutic" are intended use

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statements regarding the liposomes which are provided. Since Zalipsky and Watanabe “provide” liposomes containing the claimed compounds, Zalipsky and Watanabe meet the claims.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS